Complete Summary

GUIDELINE TITLE

Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma.

BIBLIOGRAPHIC SOURCE(S)

Motley R, Kersey P, Lawrence C. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. Br J Dermatol 2002 Jan;146(1):18-25. [82 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Primary cutaneous squamous cell carcinoma

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Dermatology
Oncology
Plastic Surgery
Radiation Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present evidence-based guidance for the treatment of primary cutaneous squamous cell carcinoma

TARGET POPULATION

Patients with primary cutaneous squamous cell carcinoma

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Histological assessment of excised tissue

Treatment

1. Surgical excision
2. Mohs' micrographic surgery
3. Curettage and cautery
4. Cryosurgery
5. Radiotherapy
6. Elective prophylactic lymph node dissection

Management

1. Patient review by multidisciplinary oncology team
2. Assessment of metastatic potential
3. Follow-up
    - Patient self examination
    - Observation by physician
4. Access to palliative care, where appropriate

MAJOR OUTCOMES CONSIDERED

- Cure rate
- Tumour metastasis
- Tumour recurrence
- Cosmetic appearance
- Morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

II-I: Evidence obtained from well designed controlled trials without randomization

II-ii: Evidence obtained from well designed cohort or case-control analytic studies, preferably from more than one centre or research group

II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length or comprehensiveness of follow-up or conflicts of evidence)

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation Grades

A. There is good evidence to support the use of the procedure.
B. There is fair evidence to support the use of the procedure.
C. There is poor evidence to support the use of the procedure.
D. There is fair evidence to support the rejection of the use of the procedure.
E. There is good evidence to support the rejection of the use of the procedure.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines are edited by the Therapy Guidelines and Audit Sub-committee (TGA) and subsequently returned to the task force for revision. The approved draft version is published in the quarterly British Association of Dermatologists (BAD) newsletter, and all BAD members are given the opportunity to respond, positively or negatively, but hopefully helpfully, within three months of publication. Finalised guidelines are approved by the TGA and the Executive Committee of the BAD and finally published in the British Journal of Dermatology.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (I-IV) and strength of recommendation ratings (A-D) are defined at the end of the "Major Recommendations" field.

Diagnosis

The diagnosis is established histologically. The histology report should include the following: pathological pattern (e.g., "adenoid type") cell morphology (e.g., "spindle cell squamous cell carcinoma [SCC]"), degree of differentiation ("well

differentiated" or "poorly differentiated"), histological grade (as described by Broders, see Appendix 2 of the original guideline document), depth (thickness in mm), the level of dermal invasion (as Clark's levels, excluding layers of surface keratin), and the presence or absence of perineural, vascular, or lymphatic invasion. The margins of the excised tissue should be stained prior to tissue preparation to allow their identification histologically and comment should be made on the lateral and deep margins of excision.

Treatment

In interpreting and applying guidelines for treatment of SCC, three important points should be noted:

- There is a lack of randomized controlled trials (RCTs) for the treatment of primary cutaneous SCC.
- There is widely varying malignant behaviour in those tumours that fall within the histological diagnostic category of "primary cutaneous SCC."
- There are varied experiences among the different specialists treating these tumours; these are determined by referral patterns and interests. Plastic and maxillofacial surgeons may encounter predominantly high-risk, aggressive tumours, whereas dermatologists may deal predominantly with smaller and less aggressive lesions.

However, there are three main factors that influence treatment, which are:

- The need for complete removal or treatment of the primary tumour
- The possible presence of local 'in transit' metastases
- The tendency of metastases to spread by lymphatics to lymph nodes

The majority of SCCs are low risk and amenable to various forms of treatment, but it is essential to identify the significant proportion that are high risk. These may be best managed by a multiprofessional team with experience of treating the most malignant tumours.

The goal of treatment is complete (preferably histologically confirmed) removal or destruction of the primary tumour and of any metastases. In order to achieve this, the margins of the tumour must be identified. The gold standard for identification of tumour margins is histological assessment, but most treatments rely on clinical judgement. It must be recognized that this is not always an accurate predictor of tumour extent, particularly where the margins of the tumour are ill-defined.

SCC may give rise to local metastases, which are discontinuous with the primary tumour. Such "in-transit" metastases may be removed by wide surgical excision or destroyed by irradiation of a wide field around the primary lesion. Small margins may not remove metastases in the vicinity of the primary tumour. Locally recurrent tumour may arise either due to failure to treat the primary continuous body of tumour or from local metastases.

SCC usually spreads to local lymph nodes, and clinically enlarged nodes should be examined histologically (for example by fine needle aspiration or excisional

biopsy). Tumour-positive lymph nodes are usually managed by regional node dissection, but detailed discussion of the management of metastatic disease is beyond the scope of these guidelines.

In the absence of clinically enlarged nodes, techniques such as high resolution ultrasound-guided fine needle aspiration cytology may be useful in evaluating regional lymph nodes in patients with high risk tumours. The role of sentinel lymph node biopsy has not been established.

Although there are many large series in which long-term outcome after treatment for cutaneous SCC has been reported, there are no large prospective randomized studies in which different treatments for this tumour have been compared.

Guidelines for Patient Treatment

Conclusions from population-based studies do not necessarily indicate the best treatment for an individual patient. In particular, when choosing a treatment modality it is important to be aware of the factors that may influence success. Curettage and cautery, cryosurgery, and to a lesser degree radiotherapy, are all techniques in which the outcome depends of the experience of the physician. Although the same could be said of surgical excision and Mohs' micrographic surgery, these two modalities provide tissue for histological examination that allows the pathologist to assess the adequacy of treatment and for the physician to undertake further surgery if necessary. For this reason, where feasible, surgical excision (including Mohs' micrographic surgery where appropriate) should be regarded as the treatment of first choice for cutaneous SCC. The other techniques can yield excellent results in experienced hands, but the quality of treatment cannot be assured or audited contemporaneously by a third party.

Surgical Excision

Surgical excision is the treatment of choice for the majority of cutaneous SCC. It allows full characterization of the tumour and a guide to the adequacy of treatment through histological examination of the margins of the excised tissue.

When undertaking surgical excision a margin of normal skin is excised from around the tumour. For clinically well-defined, low-risk tumours less than 2 cm in diameter, surgical excision with a minimum 4-mm margin around the tumour border is appropriate and would be expected to completely remove the primary tumour mass in 95% of cases (Strength of recommendation A, Quality of evidence II-iii). Narrower margins of excision are more likely to leave residual tumour. In order to maintain the same degree of confidence of adequate excision, larger tumours, high risk tumour of Broders' grade 2, 3, or 4, tumours extending into the subcutaneous tissue, and those in high-risk locations (ear, lip, scalp, eyelids, nose) should be removed with a wider margin (6 mm or more) and the tissue margins examined histologically, or with Mohs' micrographic surgery.

It is only meaningful to consider such margins when the peripheral boundary of the tumour appears clinically well-defined. The concept of a '"surgical margin" (i.e., normal-appearing tissue around the tumour) is based upon an assumption that the clinically visible margin of the tumour bears a predictable relationship to the true extent of the tumour and that excision of a margin of clinically normal-

appearing tissue around the tumour will encompass any microscopic tumour extension. The wider the surgical margin, the greater the likelihood that all tumour will be removed. Large tumours have greater microscopic tumour extension and should be removed with a wider margin. This concept is equally valid for non-surgical treatments such as radiotherapy and cryotherapy in which a margin of clinically normal-appearing tissue is treated around the tumour. Mohs' micrographic surgery does not make this assumption but displays the margins of the tissue for histological examination and allows a primary tumour mass, growing in-continuity, to be excised completely with minimal loss of normal tissue. There are important lessons to be learned from the experiences of micrographic surgery in treating cutaneous SCC (see below).

Local Metastases

Microscopic metastases may be found around high risk primary cutaneous SCC. Under these circumstances a "wide" surgical margin extending well beyond the primary tumour may include such metastases and thus have a higher cure rate than a narrower margin. Mohs' micrographic surgery removes tumour growing in continuity but does not identify in-transit micrometastases. For this reason some practitioners of Mohs' micrographic surgery will excise a further surgical margin when treating high risk tumours after the Mohs' surgical wound has been histologically confirmed to be clear of the primary tumour mass.

Histological Assessment of Surgical Margins

Conventional histological examination of one or more transverse sections of excised tissue displays a cross-section of the tumour and tissue margins. This is the best way of assessing and categorizing the nature of the tumour, and it is usual to comment on whether the tumour extends to the tissue margin, or if not, to record the margin of uninvolved skin around the tumour. The value of such comments depends on how closely the section examined reflects the excised tissue in general. If SCC appears to extend to the margin of the examined tissue, then it should be assumed, particularly if the true margin of the tissue has been stained prior to sectioning, that excision is incomplete. Orientating markers or sutures should be placed in the surgical specimen by the surgeon to allow the pathologist to report accurately on the location of any residual tumour. A pathologist, using the conventional "breadloaf" technique for examining tissue, typically views only a small sample of the specimen microscopically, and this may allow incompletely excised high-risk tumours to go undetected. There are several alternative tissue preparations that allow the peripheral margins of the excised tissue to be more comprehensively examined. The clinician and pathologist must work closely together in order to ensure appropriate sampling and microscopic examination of excised tissue, particularly with high-risk tumours.

Mohs' micrographic surgery differs because the tissue is not displayed in cross-section and, if the first level of excision is adequate, tumour may not be seen at all in the microscopic sections. There are technical factors that may occasionally hamper identification of SCC in frozen sections, and under these circumstances final histological examination should be undertaken on formalin-fixed tissue.

Mohs' Micrographic Surgery

Mohs' micrographic surgery allows precise definition and excision of primary tumour growing in-continuity, and as such would be expected to reduce errors in primary treatment that may arise due to clinically invisible tumour extension. There is good evidence that the incidence of local recurrent and metastatic disease are low after Mohs' micrographic surgery, and it should therefore be considered in the surgical treatment of high-risk SCC, particularly at difficult sites where wide surgical margins may be technically difficult to achieve without functional impairment (B, II-iii). The best cure rates for high-risk SCCs are reported in series treated by Mohs' micrographic surgery. Where Mohs' micrographic surgery is indicated but not available then one of the other histological techniques to examine the peripheral margin of the excised tissue should be employed.

However, there are no prospective randomized studies comparing therapeutic outcome between conventional or wide surgical excision vs. Mohs' micrographic surgery for cutaneous SCC.

It is firmly established that incomplete surgical excision is associated with a worse prognosis and, when doubt exists as to the adequacy of excision at the time of surgery, it is desirable, where practical, to delay or modify wound repair until complete tumour removal has been confirmed histologically.

Curettage and Cautery

Excellent cure rates have been reported in several series and experience suggests that small (<1 cm), well-differentiated, primary, slow-growing tumours arising on sun-exposed sites can be removed by experienced physicians with curettage. There are few published data relating outcome after curettage of larger tumours and different clinical tumour types.

The high cure rates reported following curettage and cautery of cutaneous SCC (II-iii) may reflect case selection, with a greater proportion of small tumours treated by curettage than by other techniques, but also raise the question as to whether curettage per se has a therapeutic advantage. The experienced clinician undertaking curettage can detect tumour tissue by its soft consistency and this may be of benefit in identifying invisible tumour extension and ensuring adequate treatment. Conventionally, cautery or electrodesiccation is applied to the curetted wound and the curettage-cautery cycle then repeated once or twice. In principle, curettage could be combined with other treatments such as surgical excision, cryotherapy, or radiotherapy; it is routinely undertaken to "debulk" the tumour prior to Mohs' micrographic surgery. Curettage provides poorly orientated material for histological examination and no histological assessment of the adequacy of treatment is possible. Curettage and cautery is not appropriate treatment for locally recurrent disease.

Cryosurgery

Good short-term cure rates have been reported for small histologically confirmed SCC treated by cryosurgery in experienced hands. Prior biopsy is necessary to establish the diagnosis histologically. There is great variability in the use of liquid nitrogen for cryotherapy and significant transatlantic variations in practice. For this reason caution should be exercised in the use of cryotherapy for SCC,

although it may be an appropriate technique for selected cases in specialized centres. Cryosurgery is not appropriate for locally recurrent disease.

Radiotherapy

Radiation therapy alone offers reported short and long-term cure rates for SCC that are comparable with other treatments. Radiotherapy will, in certain circumstances, give the best cosmetic and/or functional result. This will often be the case for lesions arising on the lip, nasal vestibule (and sometimes the outside of the nose), and ear, among others. Certain very advanced tumours, where surgical morbidity would be unacceptably high, may also be best treated by radiotherapy.

Elective Prophylactic Lymph Node Dissection

Elective prophylactic lymph node dissection has been proposed for SCC on the lip greater than 6 mm in depth and cutaneous SCC greater than 8 mm in depth, but evidence for this is weak (C, II-iii). Elective lymph node dissection is not routinely practised and there is no compelling evidence of benefit over morbidity.

Summary of Treatment Options for Primary Cutaneous Squamous Cell Carcinoma

Treatment	Indications	Notes
Surgical excision	All resectable tumours	• Generally treatment of choice for SCC • High-risk tumours need wide margins or histological margin control
Mohs' micrographic surgery/excision with histological control	High-risk tumours, recurrent tumours	Treatment of choice for high-risk tumours
Radiotherapy	Non-resectable tumours	
Curettage and cautery	Small, well-defined low-risk tumours	Curettage may be useful prior to surgical excision.
Cryotherapy	Small, well-defined, low-risk tumours	Only suitable for experienced practitioners

The Multiprofessional Oncology Team

Patients with high risk SCC and those presenting with clinically involved lymph nodes should ideally be reviewed by a multiprofessional oncology team which includes a dermatologist, pathologist, appropriately trained surgeon (usually a plastic or maxillofacial surgeon), clinical oncologist, and a clinical nurse specialist in skin cancer. Some advanced tumours are not surgically resectable and these should be managed in a multiprofessional setting in order that other therapeutic options are considered. Patients should be provided with suitable written information concerning diagnosis, prognosis and follow-up support, local and

national support organizations, and, where appropriate, access to a multiprofessional palliative care team.

Follow-Up

Early detection and treatment improves survival of patients with recurrent disease. Ninety-five percent of local recurrences and 95% of metastases are detected within 5 years. It would therefore seem reasonable for the patient who has had a high-risk SCC to be kept under observation for recurrent disease for this period of time (A, II-ii). Patients should be, as far as possible, instructed in self-examination. Observation for recurrent disease may be undertaken by the specialist, primary care physician, or patient self-examination. The decision as to who follows the patient will depend upon the disease risk, local facilities, and interests.

Definitions:

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

II-I: Evidence obtained from well designed controlled trials without randomization

II-ii: Evidence obtained from well designed cohort or case-control analytic studies, preferably from more than one centre or research group

II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length or comprehensiveness of follow-up or conflicts of evidence)

Recommendation Grades

A. There is good evidence to support the use of the procedure.
B. There is fair evidence to support the use of the procedure.
C. There is poor evidence to support the use of the procedure.
D. There is fair evidence to support the rejection of the use of the procedure.
E. There is good evidence to support the rejection of the use of the procedure

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Optimal treatment for patients with primary cutaneous squamous cell carcinoma

POTENTIAL HARMS

Not stated

CONTRAINDICATIONS

CONTRAINDICATIONS

- Surgical excision is contraindicated when surgical morbidity is likely to be unreasonably high.
- Mohs' micrographic surgery/excision with histological control is contraindicated when surgical morbidity is likely to be unreasonably high.
- Radiotherapy is contraindicated when tumour margins are ill-defined.
- Curettage and cautery is contraindicated for high-risk tumours.
- Cryotherapy is contraindicated for high-risk tumours and recurrent tumours.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines, prepared on behalf of the British Association of Dermatologists, the British Association of Plastic Surgeons and in consultation with members of the Faculty of Clinical Oncology of the Royal College of Radiologists, reflect the best published data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not be necessarily deemed negligent.
- In interpreting and applying guidelines for treatment of squamous cell carcinoma (SCC), three important points should be noted:
    - There is a lack of randomized controlled trials (RCTs) for the treatment of primary cutaneous SCC.

    - There is widely varying malignant behaviour in those tumours that fall within the histological diagnostic category of "primary cutaneous SCC."
    - There are varied experiences among the different specialists treating these tumours; these are determined by referral patterns and interests. Plastic and maxillofacial surgeons may encounter predominantly high-risk, aggressive tumours, whereas dermatologists may deal predominantly with smaller and less aggressive lesions.
- Although there are many large series in which long-term outcome after treatment for cutaneous SCC has been reported, there are no large prospective randomized studies in which different treatments for this tumour have been compared.
- Conclusions from population-based studies do not necessarily indicate the best treatment for an individual patient. In particular, when choosing a treatment modality it is important to be aware of the factors that may influence success.
- It is important that these guidelines are used appropriately in that they can only assist the practitioner and cannot be used to mandate, authorise, or outlaw treatment options. Of course it is the responsibility of the practising clinician to interpret the application of guidelines, taking into account local circumstances.
- Guidelines are inherently a fluid, dynamic process and will be updated on the British Association of Dermatologists (BAD) Web site on a regular basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Motley R, Kersey P, Lawrence C. Multiprofessional guidelines for the management of the patient with primary cutaneous squamous cell carcinoma. Br J Dermatol 2002 Jan;146(1):18-25. [82 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Jan

GUIDELINE DEVELOPER(S)

British Association of Dermatologists

SOURCE(S) OF FUNDING

British Association of Dermatologists

GUIDELINE COMMITTEE

British Association of Dermatologists Therapy Guidelines and Audit Subcommittee

The Multiprofessional Skin Cancer Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the British Association of Dermatologists Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Griffiths CE. The British Association of Dermatologists guidelines for the management of skin disease Br J Dermatol. 1999 Sep;141(3):396-7.

Electronic copies: Available in Portable Document Format (PDF) from the British Association of Dermatologists Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 22, 2005. The information was verified by the guideline developer on June 27, 2005.

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DISCLAIMER

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